

SYR-HDAC-5005-U.ST25
SEQUENCE LISTING

<110> Syrrx, Inc.

<120> HISTONE DEACETYLASE INHIBITORS

<130> SYR-HDAC-5005-U

<140> Not Yet Assigned

<141> 2004-03-17

<150> US 60/455,437

<151> 2003-03-17

<150> US 60/531,203

<151> 2003-12-19

<160> 8

<170> PatentIn version 3.2

<210> 1

<211> 513

<212> PRT

<213> Custom

<220>

<221> Residues 1-482 of HDAC1 and a 6-histidine tag at the N-terminus

<222> (1)..(513)

<400> 1

Met Ser Tyr Tyr His His His His His His Asp Tyr Asp Ile Pro Thr
1 5 10 15

Thr Glu Asn Leu Tyr Phe Gln Gly Ala Met Glu Pro Gly Gly Ser Met
20 25 30

Ala Gln Thr Gln Gly Thr Arg Arg Lys Val Cys Tyr Tyr Tyr Asp Gly
35 40 45

Asp Val Gly Asn Tyr Tyr Tyr Gly Gln Gly His Pro Met Lys Pro His
50 55 60

Arg Ile Arg Met Thr His Asn Leu Leu Leu Asn Tyr Gly Leu Tyr Arg
65 70 75 80

Lys Met Glu Ile Tyr Arg Pro His Lys Ala Asn Ala Glu Glu Met Thr
85 90 95

Lys Tyr His Ser Asp Asp Tyr Ile Lys Phe Leu Arg Ser Ile Arg Pro
100 105 110

Asp Asn Met Ser Glu Tyr Ser Lys Gln Met Gln Arg Phe Asn Val Gly
115 120 125

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Glu Asp Cys Pro Val Phe Asp Gly Leu Phe Glu Phe Cys Gln Leu Ser
 130 135 140
 Thr Gly Gly Ser Val Ala Ser Ala Val Lys Leu Asn Lys Gln Gln Thr
 145 150 155 160
 Asp Ile Ala Val Asn Trp Ala Gly Gly Leu His His Ala Lys Lys Ser
 165 170 175
 Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp Ile Val Leu Ala Ile Leu
 180 185 190
 Glu Leu Leu Lys Tyr His Gln Arg Val Leu Tyr Ile Asp Ile Asp Ile
 195 200 205
 His His Gly Asp Gly Val Glu Glu Ala Phe Tyr Thr Thr Asp Arg Val
 210 215 220
 Met Thr Val Ser Phe His Lys Tyr Gly Glu Tyr Phe Pro Gly Thr Gly
 225 230 235 240
 Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly Lys Tyr Tyr Ala Val Asn
 245 250 255
 Tyr Pro Leu Arg Asp Gly Ile Asp Asp Glu Ser Tyr Glu Ala Ile Phe
 260 265 270
 Lys Pro Val Met Ser Lys Val Met Glu Met Phe Gln Pro Ser Ala Val
 275 280 285
 Val Leu Gln Cys Gly Ser Asp Ser Leu Ser Gly Asp Arg Leu Gly Cys
 290 295 300
 Phe Asn Leu Thr Ile Lys Gly His Ala Lys Cys Val Glu Phe Val Lys
 305 310 315 320
 Ser Phe Asn Leu Pro Met Leu Met Leu Gly Gly Gly Gly Tyr Thr Ile
 325 330 335
 Arg Asn Val Ala Arg Cys Trp Thr Tyr Glu Thr Ala Val Ala Leu Asp
 340 345 350
 Thr Glu Ile Pro Asn Glu Leu Pro Tyr Asn Asp Tyr Phe Glu Tyr Phe
 355 360 365
 Gly Pro Asp Phe Lys Leu His Ile Ser Pro Ser Asn Met Thr Asn Gln
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370

375

380

Asn Thr Asn Glu Tyr Leu Glu Lys Ile Lys Gln Arg Leu Phe Glu Asn
385 390 395 400

Leu Arg Met Leu Pro His Ala Pro Gly Val Gln Met Gln Ala Ile Pro
405 410 415

Glu Asp Ala Ile Pro Glu Glu Ser Gly Asp Glu Asp Glu Asp Asp Pro
420 425 430

Asp Lys Arg Ile Ser Ile Cys Ser Ser Asp Lys Arg Ile Ala Cys Glu
435 440 445

Glu Glu Phe Ser Asp Ser Glu Glu Glu Gly Glu Gly Gly Arg Lys Asn
450 455 460

Ser Ser Asn Phe Lys Lys Ala Lys Arg Val Lys Thr Glu Asp Glu Lys
465 470 475 480

Glu Lys Asp Pro Glu Glu Lys Lys Glu Val Thr Glu Glu Glu Lys Thr
485 490 495

Lys Glu Glu Lys Pro Glu Ala Lys Gly Val Lys Glu Glu Val Lys Leu
500 505 510

Ala

<210> 2
<211> 1542
<212> DNA
<213> Custom

<220>
<221> DNA sequence encoding residues 1-482 of HDAC1 and a 6-histidine
tag at the N-terminus
<222> (1)..(1542)

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aaagtctgtt actactacga cggggatgtt ggaaattact attatggaca aggccacca 180
atgaagctc accgaatccg catgactcat aatttgctgc tcaactatgg tctctaccga 240
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gatgactaca ttaaattctt gcgctccatc cgtccagata acatgtcggg gtacagcaag 360

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cagatgcaga gattcaacgt tggtagaggac tgtccagtat tcgatggcct gtttgagttc 420
 tgtcagttgt ctactggtgg ttctgtggca agtgctgtga aacttaataa gcagcagacg 480
 gacatcgctg tgaattgggc tgggggcctg caccatgcaa agaagtccga ggcattctggc 540
 ttctgttacg tcaatgatat cgtcttgccc atcctggaac tgctaaagta tcaccagagg 600
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<210> 3
 <211> 498
 <212> PRT
 <213> Custom

<220>
 <221> Residues 1-488 of HDAC2 and a 6-histidine tag at the C-terminus
 <222> (1)..(498)

<400> 3

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 1 5 10 15

Tyr Tyr Tyr Asp Gly Asp Ile Gly Asn Tyr Tyr Tyr Gly Gln Gly His
 20 25 30

Pro Met Lys Pro His Arg Ile Arg Met Thr His Asn Leu Leu Leu Asn
 35 40 45

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Tyr Gly Leu Tyr Arg Lys Met Glu Ile Tyr Arg Pro His Lys Ala Thr
 50 55 60
 Ala Glu Glu Met Thr Lys Tyr His Ser Asp Glu Tyr Ile Lys Phe Leu
 65 70 75 80
 Arg Ser Ile Arg Pro Asp Asn Met Ser Glu Tyr Ser Lys Gln Met Gln
 85 90 95
 Arg Phe Asn Val Gly Glu Asp Cys Pro Val Phe Asp Gly Leu Phe Glu
 100 105 110
 Phe Cys Gln Leu Ser Thr Gly Gly Ser Val Ala Gly Ala Val Lys Leu
 115 120 125
 Asn Arg Gln Gln Thr Asp Met Ala Val Asn Trp Ala Gly Gly Leu His
 130 135 140
 His Ala Lys Lys Ser Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp Ile
 145 150 155 160
 Val Leu Ala Ile Leu Glu Leu Leu Lys Tyr His Gln Arg Val Leu Tyr
 165 170 175
 Ile Asp Ile Asp Ile His His Gly Asp Gly Val Glu Glu Ala Phe Tyr
 180 185 190
 Thr Thr Asp Arg Val Met Thr Val Ser Phe His Lys Tyr Gly Glu Tyr
 195 200 205
 Phe Pro Gly Thr Gly Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly Lys
 210 215 220
 Tyr Tyr Ala Val Asn Phe Pro Met Arg Asp Gly Ile Asp Asp Glu Ser
 225 230 235 240
 Tyr Gly Gln Ile Phe Lys Pro Ile Ile Ser Lys Val Met Glu Met Tyr
 245 250 255
 Gln Pro Ser Ala Val Val Leu Gln Cys Gly Ala Asp Ser Leu Ser Gly
 260 265 270
 Asp Arg Leu Gly Cys Phe Asn Leu Thr Val Lys Gly His Ala Lys Cys
 275 280 285
 Val Glu Val Val Lys Thr Phe Asn Leu Pro Leu Leu Met Leu Gly Gly
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300

290

295

Gly Gly Tyr Thr Ile Arg Asn Val Ala Arg Cys Trp Thr Tyr Glu Thr
305 310 315 320

Ala Val Ala Leu Asp Cys Glu Ile Pro Asn Glu Leu Pro Tyr Asn Asp
325 330 335

Tyr Phe Glu Tyr Phe Gly Pro Asp Phe Lys Leu His Ile Ser Pro Ser
340 345 350

Asn Met Thr Asn Gln Asn Thr Pro Glu Tyr Met Glu Lys Ile Lys Gln
355 360 365

Arg Leu Phe Glu Asn Leu Arg Met Leu Pro His Ala Pro Gly Val Gln
370 375 380

Met Gln Ala Ile Pro Glu Asp Ala Val His Glu Asp Ser Gly Asp Glu
385 390 395 400

Asp Gly Glu Asp Pro Asp Lys Arg Ile Ser Ile Arg Ala Ser Asp Lys
405 410 415

Arg Ile Ala Cys Asp Glu Glu Phe Ser Asp Ser Glu Asp Glu Gly Glu
420 425 430

Gly Gly Arg Arg Asn Val Ala Asp His Lys Lys Gly Ala Lys Lys Ala
435 440 445

Arg Ile Glu Glu Asp Lys Lys Glu Thr Glu Asp Lys Lys Thr Asp Val
450 455 460

Lys Glu Glu Asp Lys Ser Lys Asp Asn Ser Gly Glu Lys Thr Asp Thr
465 470 475 480

Lys Gly Thr Lys Ser Glu Gln Leu Ser Asn Pro Gly His His His His
485 490 495

His His

<210> 4
<211> 1497
<212> DNA
<213> Custom

<220>
<221> DNA sequence encoding residues 1-488 of HDAC2 and a 6-histidine
Page 6

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<222> tag at the C-terminus
(1)..(1497)

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<400> 4
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atgaccataa acttgctgtt aaattatggc ttatacagaa aaatggaaat atataggccc    180
cataaagcca ctgccgaaga aatgacaaaa taccacagtg atgagtatat caaatttcta    240
cgggtcaataa gaccagataa catgtctgag tatagtaagc agatgcagag atttaatgtt    300
ggagaagatt gtccagtgtt tgatggactc tttgagtttt gtcagctctc aactggcggt    360
tcagttgctg gagctgtgaa gttaaaccga caacagactg atatggctgt taattgggct    420
ggaggattac atcatgctaa gaaatcagaa gcatcaggat tctgttacgt taatgatatt    480
gtgcttgcca tccttgaatt actaaagtat catcagagag tcttatatat tgatatagat    540
attcatcatg gtgatggtgt tgaagaagct ttttatacaa cagatcgtgt aatgacggta    600
tcattccata aatatgggga atactttcct ggcacaggag acttgaggga tattggtgct    660
ggaaaaggca aatactatgc tgtcaatttt ccaatgagag atggtataga tgatgagtca    720
tatgggcaga tatttaagcc tattatctca aaggatgatg agatgtatca acctagtgt    780
gtggtattac agtgtggtgc agactcatta tctggtgata gactgggttg tttcaatcta    840
acagtcaaag gtcattgctaa atgtgtagaa gttgtaaaaa cttttaactt accattactg    900
atgcttggag gaggtggcta cacaatccgt aatgttgctc gatgttggac atatgagact    960
gcagttgccc ttgattgtga gattcccaat gagttgccat ataattgatta ctttgagtat   1020
tttggaccag acttcaaact gcatattagt ccttcaaaca tgacaaacca gaacactcca   1080
gaatatatgg aaaagataaa acagcgtttg tttgaaaatt tgcgcatgtt acctcatgca   1140
cctggtgtcc agatgcaagc tattccagaa gatgctgttc atgaagacag tggagatgaa   1200
gatggagaag atccagacaa gagaatttct attcgagcat cagacaagcg gatagcttgt   1260
gatgaagaat tctcagattc tgaggatgaa ggagaaggag gtcgaagaaa tgtggctgat   1320
cataagaaag gagcaaagaa agctagaatt gaagaagata agaaagaaac agaggacaaa   1380
aaaacagacg ttaaggaaga agataaatcc aaggacaaca gtggtgaaaa aacagatacc   1440
aaaggaacca aatcagaaca gctcagcaac cccgggcatc accatcacca tcactaa     1497

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<210> 5
 <211> 782
 <212> PRT
 <213> Custom

<220>
 <221> Residues 73-845 of HDAC6 and a 6-histidine tag at the C-terminus
 Page 7

<222> (1)..(782)

<400> 5

Met Pro Gly Met Asp Leu Asn Leu Glu Ala Glu Ala Leu Ala Gly Thr
 1 5 10 15

Gly Leu Val Leu Asp Glu Gln Leu Asn Glu Phe His Cys Leu Trp Asp
 20 25 30

Asp Ser Phe Pro Glu Gly Pro Glu Arg Leu His Ala Ile Lys Glu Gln
 35 40 45

Leu Ile Gln Glu Gly Leu Leu Asp Arg Cys Val Ser Phe Gln Ala Arg
 50 55 60

Phe Ala Glu Lys Glu Glu Leu Met Leu Val His Ser Leu Glu Tyr Ile
 65 70 75 80

Asp Leu Met Glu Thr Thr Gln Tyr Met Asn Glu Gly Glu Leu Arg Val
 85 90 95

Leu Ala Asp Thr Tyr Asp Ser Val Tyr Leu His Pro Asn Ser Tyr Ser
 100 105 110

Cys Ala Cys Leu Ala Ser Gly Ser Val Leu Arg Leu Val Asp Ala Val
 115 120 125

Leu Gly Ala Glu Ile Arg Asn Gly Met Ala Ile Ile Arg Pro Pro Gly
 130 135 140

His His Ala Gln His Ser Leu Met Asp Gly Tyr Cys Met Phe Asn His
 145 150 155 160

Val Ala Val Ala Ala Arg Tyr Ala Gln Gln Lys His Arg Ile Arg Arg
 165 170 175

Val Leu Ile Val Asp Trp Asp Val His His Gly Gln Gly Thr Gln Phe
 180 185 190

Thr Phe Asp Gln Asp Pro Ser Val Leu Tyr Phe Ser Ile His Arg Tyr
 195 200 205

Glu Gln Gly Arg Phe Trp Pro His Leu Lys Ala Ser Asn Trp Ser Thr
 210 215 220

Thr Gly Phe Gly Gln Gly Gln Gly Tyr Thr Ile Asn Val Pro Trp Asn
 225 230 235 240

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Gln Val Gly Met Arg Asp Ala Asp Tyr Ile Ala Ala Phe Leu His Val
245 250 255

Leu Leu Pro Val Ala Leu Glu Phe Gln Pro Gln Leu Val Leu Val Ala
260 265 270

Ala Gly Phe Asp Ala Leu Gln Gly Asp Pro Lys Gly Glu Met Ala Ala
275 280 285

Thr Pro Ala Gly Phe Ala Gln Leu Thr His Leu Leu Met Gly Leu Ala
290 295 300

Gly Gly Lys Leu Ile Leu Ser Leu Glu Gly Gly Tyr Asn Leu Arg Ala
305 310 315 320

Leu Ala Glu Gly Val Ser Ala Ser Leu His Thr Leu Leu Gly Asp Pro
325 330 335

Cys Pro Met Leu Glu Ser Pro Gly Ala Pro Cys Arg Ser Ala Gln Ala
340 345 350

Ser Val Ser Cys Ala Leu Glu Ala Leu Glu Pro Phe Trp Glu Val Leu
355 360 365

Val Arg Ser Thr Glu Thr Val Glu Arg Asp Asn Met Glu Glu Asp Asn
370 375 380

Val Glu Glu Ser Glu Glu Glu Gly Pro Trp Glu Pro Pro Val Leu Pro
385 390 395 400

Ile Leu Thr Trp Pro Val Leu Gln Ser Arg Thr Gly Leu Val Tyr Asp
405 410 415

Gln Asn Met Met Asn His Cys Asn Leu Trp Asp Ser His His Pro Glu
420 425 430

Val Pro Gln Arg Ile Leu Arg Ile Met Cys Arg Leu Glu Glu Leu Gly
435 440 445

Leu Ala Gly Arg Cys Leu Thr Leu Thr Pro Arg Pro Ala Thr Glu Ala
450 455 460

Glu Leu Leu Thr Cys His Ser Ala Glu Tyr Val Gly His Leu Arg Ala
465 470 475 480

Thr Glu Lys Met Lys Thr Arg Glu Leu His Arg Glu Ser Ser Asn Phe
485 490 495

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Asp Ser Ile Tyr Ile Cys Pro Ser Thr Phe Ala Cys Ala Gln Leu Ala
500 505 510

Thr Gly Ala Ala Cys Arg Leu Val Glu Ala Val Leu Ser Gly Glu Val
515 520 525

Leu Asn Gly Ala Ala Val Val Arg Pro Pro Gly His His Ala Glu Gln
530 535 540

Asp Ala Ala Cys Gly Phe Cys Phe Phe Asn Ser Val Ala Val Ala Ala
545 550 555 560

Arg His Ala Gln Thr Ile Ser Gly His Ala Leu Arg Ile Leu Ile Val
565 570 575

Asp Trp Asp Val His His Gly Asn Gly Thr Gln His Met Phe Glu Asp
580 585 590

Asp Pro Ser Val Leu Tyr Val Ser Leu His Arg Tyr Asp His Gly Thr
595 600 605

Phe Phe Pro Met Gly Asp Glu Gly Ala Ser Ser Gln Ile Gly Arg Ala
610 615 620

Ala Gly Thr Gly Phe Thr Val Asn Val Ala Trp Asn Gly Pro Arg Met
625 630 635 640

Gly Asp Ala Asp Tyr Leu Ala Ala Trp His Arg Leu Val Leu Pro Ile
645 650 655

Ala Tyr Glu Phe Asn Pro Glu Leu Val Leu Val Ser Ala Gly Phe Asp
660 665 670

Ala Ala Arg Gly Asp Pro Leu Gly Gly Cys Gln Val Ser Pro Glu Gly
675 680 685

Tyr Ala His Leu Thr His Leu Leu Met Gly Leu Ala Ser Gly Arg Ile
690 695 700

Ile Leu Ile Leu Glu Gly Gly Tyr Asn Leu Thr Ser Ile Ser Glu Ser
705 710 715 720

Met Ala Ala Cys Thr Arg Ser Leu Leu Gly Asp Pro Pro Pro Leu Leu
725 730 735

Thr Leu Pro Arg Pro Pro Leu Ser Gly Ala Leu Ala Ser Ile Thr Glu
Page 10

740 SYR-HDAC-5005-U.ST25 750
745

Thr Ile Gln Val His Arg Arg Tyr Trp Arg Ser Leu Arg Val Met Lys
755 760 765

Val Glu Asp Arg Glu Gly Pro Gly His His His His His His
770 775 780

<210> 6
<211> 2349
<212> DNA
<213> Custom

<220>
<221> DNA encoding residues 73-845 of HDAC6 and a 6-histidine tag at
the C-terminus
<222> (1)..(2349)

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cggctccatg ccatcaagga gcaactgac caggagggcc tcctagatcg ctgcgtgtcc      180
tttcaggccc ggtttgctga aaaggaagag ctgatgttg ttcacagcct agaatatatt      240
gatctgatgg aaacaacca gtacatgaat gagggagaac tccgtgtcct agcagacacc      300
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cttgagccct tctgggaggt tcttgtgaga tcaactgaga ccgtggagag ggacaacatg     1140
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atgtgccgtc tggaggagct gggccttgcc gggcgctgcc tcaccctgac accgcgcctt 1380
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catcactaa 2349

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<210> 7
 <211> 385
 <212> PRT
 <213> Custom

<220>
 <221> Residues 1-377 of HDAC8 and a 6-histidine tag at the N-terminus
 <222> (1)..(385)
 <400> 7

Met His His His His His His Pro Met Glu Glu Pro Glu Glu Pro Ala
 1 5 10 15

Asp Ser Gly Gln Ser Leu Val Pro Val Tyr Ile Tyr Ser Pro Glu Tyr
 20 25 30

Val Ser Met Cys Asp Ser Leu Ala Lys Ile Pro Lys Arg Ala Ser Met
 35 40 45

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Val His Ser Leu Ile Glu Ala Tyr Ala Leu His Lys Gln Met Arg Ile
50 55 60

Val Lys Pro Lys Val Ala Ser Met Glu Glu Met Ala Ala Phe His Thr
65 70 75 80

Asp Ala Tyr Leu Gln His Leu Gln Lys Val Ser Gln Glu Gly Asp Asp
85 90 95

Asp His Pro Asp Ser Ile Glu Tyr Gly Leu Gly Tyr Asp Cys Pro Ala
100 105 110

Thr Glu Gly Ile Phe Asp Tyr Ala Ala Ala Ile Gly Gly Ala Thr Ile
115 120 125

Thr Ala Ala Gln Cys Leu Ile Asp Gly Met Cys Lys Val Ala Ile Asn
130 135 140

Trp Ser Gly Gly Trp His His Ala Lys Lys Asp Glu Ala Ser Gly Phe
145 150 155 160

Cys Tyr Leu Asn Asp Ala Val Leu Gly Ile Leu Arg Leu Arg Arg Lys
165 170 175

Phe Glu Arg Ile Leu Tyr Val Asp Leu Asp Leu His His Gly Asp Gly
180 185 190

Val Glu Asp Ala Phe Ser Phe Thr Ser Lys Val Met Thr Val Ser Leu
195 200 205

His Lys Phe Ser Pro Gly Phe Phe Pro Gly Thr Gly Asp Val Ser Asp
210 215 220

Val Gly Leu Gly Lys Gly Arg Tyr Tyr Ser Val Asn Val Pro Ile Gln
225 230 235 240

Asp Gly Ile Gln Asp Glu Lys Tyr Tyr Gln Ile Cys Glu Ser Val Leu
245 250 255

Lys Glu Val Tyr Gln Ala Phe Asn Pro Lys Ala Val Val Leu Gln Leu
260 265 270

Gly Ala Asp Thr Ile Ala Gly Asp Pro Met Cys Ser Phe Asn Met Thr
275 280 285

Pro Val Gly Ile Gly Lys Cys Leu Lys Tyr Ile Leu Gln Trp Gln Leu
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290

295

Ala Thr Leu Ile Leu Gly Gly Gly Gly Tyr Asn Leu Ala Asn Thr Ala
305 310 315 320

Arg Cys Trp Thr Tyr Leu Thr Gly Val Ile Leu Gly Lys Thr Leu Ser
325 330 335

Ser Glu Ile Pro Asp His Glu Phe Phe Thr Ala Tyr Gly Pro Asp Tyr
340 345 350

Val Leu Glu Ile Thr Pro Ser Cys Arg Pro Asp Arg Asn Glu Pro His
355 360 365

Arg Ile Gln Gln Ile Leu Asn Tyr Ile Lys Gly Asn Leu Lys His Val
370 375 380

Val
385

<210> 8
<211> 1158
<212> DNA
<213> Custom

<220>
<221> DNA encoding residues 1-377 of HDAC8 and a 6-histidine tag at the
N-terminus
<222> (1)..(1158)

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cagatgagga tagttaagcc taaagtggcc tccatggagg agatggccgc cttccacact 240
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